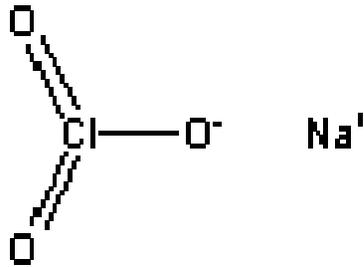


Sodium Chlorate



- Oxidizing agent
- By-product in drinking water disinfected with chlorine dioxide
- Widespread human exposure from drinking water

Study Design

- Male and female F344 rats and B6C3F₁ mice
- Drinking water route of exposure

- 3-Week Dose Groups
 - 0, 125, 250, 500, 1,000, or 2,000 mg/L

- 2-Year Dose Groups
 - Rats- 0, 125, 1,000, or 2,000 mg/L
 - Mice- 0, 500, 1,000, or 2,000 mg/L

- Negative in *Salmonella* (+/- S9)
- Negative in micronucleus assay

Results of 3-Week Studies in Rats

- All rats survived to the end of the study
- Mean body weights and water consumption were similar to controls
- Increased incidences of thyroid gland follicular cell hypertrophy in males and female exposed to ≥ 500 mg/L

Results of 2-Year Studies in Rats

- Survival, mean body weights, and water consumption were similar to controls
- Thyroid hormone concentrations:
 - Special study rats
 - $\downarrow T_3$, $\downarrow T_4$, and $\uparrow TSH$
 - Day 4- 1,000 or 2,000 mg/L males and females
 - Week 3- 2,000 mg/L males and females
 - $\uparrow TSH$
 - Week 13- 2,000 mg/L males and females

Thyroid Gland Follicular Cell Hypertrophy

Special Study Rats

Concentration (mg/L) ^a	0	125	1,000	2,000
<u>Male</u>				
Week 3	0	0	10** (2.0)	10** (2.0)
Week 13	0	0	10** (2.0)	10** (2.0)
<u>Female</u>				
Week 3	0	0	10** (2.0)	10** (2.0)
Week 13	0	0	10** (1.0)	10** (2.0)

^aN=10

**P≤0.01

Thyroid Gland Lesions in the 2-year Study

Concentration (mg/L)	0	125	1,000	2,000
Male	(47)	(44)	(43)	(47)
Hypertrophy	4 (1.3)	13* (1.2)	33** (1.5)	40** (2.0)
Adenoma	1	0	0	2
Carcinoma	0	0	0	4
Adenoma or Carcinoma	1	0	0	6
Female	(47)	(47)	(43)	(46)
Hypertrophy	3 (1.3)	7 (1.0)	27** (1.2)	42** (1.8)
Mineralization	25 (1.0)	26 (1.0)	40** (1.3)	44** (2.1)
Adenoma	0	0	0	2
Carcinoma	1	0	1	2
Adenoma or Carcinoma	1	0	1	4

* $P \leq 0.05$

** $P \leq 0.01$

Nonneoplastic Effects in Male Rats

Concentration (mg/L)	0	125	1,000	2,000
<u>Bone marrow</u> Hyperplasia	(48) 28 (1.9)	(48) 35 (2.3)	(50) 41** (2.4)	(49) 40* (2.7)
<u>Spleen</u> Hematopoietic cell proliferation	(48) 2 (2.5)	(49) 6 (2.3)	(49) 4 (2.5)	(50) 11** (2.5)

* $P \leq 0.05$

** $P \leq 0.01$

Results of 3-Week Studies in Mice

- All mice survived to the end of the study
- Mean body weights were similar to controls
- Water consumption was similar to controls

Results of 2-Year Studies in Mice

- Survival and water consumption were similar to controls
- Mean body weights of males were similar to controls
- Mean body weights were decreased for females exposed to ≥ 500 mg/L

Pancreatic Islet Lesions in the 2-year Study

Concentration (mg/L)	0	500	1,000	2,000
<u>Male</u>	(48)	(50)	(50)	(50)
Hyperplasia	31 (2.4)	25 (2.3)	28 (2.5)	23 (2.3)
<u>Female</u>	(46)	(47)	(49)	(49)
Hyperplasia	9 (1.7)	6 (2.0)	4 (2.3)	3 (2.0)
Adenoma	0	2	2	3
Carcinoma	0	0	0	1
Adenoma or Carcinoma	0	2	2	4

Nonneoplastic Effects in Female Mice

Concentration (mg/L)	0	500	1,000	2,000
<u>Thyroid Gland</u> Follicular cell hypertrophy	(48) 3 (1.3)	(50) 2 (2.0)	(49) 5 (1.0)	(50) 14** (1.4)
<u>Bone marrow</u> Hyperplasia	(50) 14 (2.4)	(50) 28** (2.6)	(50) 29** (2.9)	(50) 31** (2.7)

**P≤0.01

Conclusions- Rats

- *Some evidence of carcinogenic activity* of sodium chlorate in male and female F344/N rats based on increased incidences of thyroid gland neoplasms
- Increased incidences of nonneoplastic lesions:
 - Follicular cell hypertrophy- males and females
 - Follicular cell mineralization- females
 - Bone marrow hyperplasia- males
 - Hematopoietic cell proliferation -males

Conclusions- Mice

- No evidence of carcinogenic activity of sodium chlorate in male B6C3F₁ mice exposed to 500, 1,000, or 2,000 mg/L
- *Equivocal evidence of carcinogenic activity of sodium chlorate in female B6C3F₁ mice based on marginally increased incidences of pancreatic islet neoplasms*
- Increased incidences of nonneoplastic lesions:
 - Follicular cell hypertrophy- females
 - Bone marrow hyperplasia- females